REMARKS

Claims:

Claims 8-11, 13-16, and 18-19 are under consideration in the present application. Claims 1-7, 12, 17, and 20-49 are herein canceled due to restriction requirement and Applicants reserve the right to file divisional applications or take other appropriate measures deemed necessary to protect the inventions in the canceled claims without prejudice thereon.

Claims 8 and 13 are herein amended by addition of "*Magnaporthe*" to steps (a) and (b) of each. Support for the amendment is found in original Claims 10 and 15, as well as throughout the specification as originally filed. Claims 8 and 13 are also amended at part (b) to correct antecedent basis by insertion of the term "the". Claims 10, 15, 18 and 19 are canceled. Claims 11 and 16 are in condition for allowance as originally submitted. Accordingly, no new matter is added.

I. Claim Rejections - 35 USC § 112

Claims 10-11 and 15-16 are rejected under 35 USC § 112 as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner states that the fungus *Magnaporthe* must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. Applicants respectfully point out that *Magnaporthe grisea* strain Guy11 is available from the American Type Culture Collection (ATCC) as strain number ATCC 201236. Accordingly, Applicants respectfully request that the 35 U.S.C. § 112, 1st paragraph, rejection of Claims 11 and 16 be withdrawn. Cancellation of Claims 10 and 15 herein obviates the rejection based on Claims 10 and 15.

Claims 18-19 are rejected under 35 USC § 112, first paragraph because "the claims are non-enabling for the scope of that claim." Cancellation of Claims 18 and 19 herein obviates the rejection based on Claims 18 and 19.

II. Claim Rejections - 35 USC § 102

Claims 8 and 13 are rejected under 35 USC § 102(b) as anticipated by Bode et

al. Claim 13 is rejected under 35 USC § 102(b) as anticipated by Grandoni with evidence from IUBMB Enzyme Nomenclature Classification, and also as anticipated by Hawkes et al. with evidence from IUBMB Enzyme Nomenclature Classification. Applicants respectfully disagree with the 35 U.S.C. § 102(b) rejections and request reconsideration in light of the present amendment and the remarks that follow.

Bode et al. teach a method for identifying an inhibitor of 3-isopropylmalate dehydratase in *Candida.* Applicants' claimed invention is directed to methods for identifying compounds as candidate antibiotics by measuring the ability of test compounds to inhibit the enzymatic activity of a 3-isopropylmalate dehydratase, and further determining the ability of the inhibitory compounds to reduce the pathogenicity of an organism. The present application discloses that the pathogenicity of *Magnaporthe* was severely reduced when the activity of a *Magnaporthe* 3-isopropylmalate dehydratase was knocked out, an unexpected result indicating 3-isopropylmalate dehydratase as a target for the identification of antibiotics.

As taught in Applicants' specification on pages 3 and 4, it is not possible to predict the outcome of disruption of a particular biochemical pathway in any given fungus, even when a similar result is known from another fungal species. Specifically, "it is not currently possible to determine which specific growth materials may be readily obtained by a pathogen from its host, and which materials may not." (Hamer et al., page 4, lines 16-18). The products of biochemical pathways may be obtainable by more than one pathway route, so that if one route is disrupted, the end product may be obtained by an alternative route. Additionally, species of pathogenic fungi differ in their ability to obtain materials from a host, thus making it possible for a fungus to by-pass a biochemical pathway disruption by obtaining the end product of the biochemical pathway directly from the host organism.

The uncertainty of the outcome of pathway disruption is supported in the Bode reference. In the abstract, Bode states that "[i]n yeasts and fungi, knowledge of the kinetic and regulatory properties of the enzyme is not extensive and includes only *Saccaromyces cerevisiae* and *Neurospora crassa*. From studies with these organisms it has been documented that there are similarities but also differences of the enzyme properties." (Bode et al., page 21 lines 15-19). Because of the uncertainty of the effect of

a pathway disruption in a particular fungus, Bode et al., examining *Candida,* cannot be applied to Applicants' finding in *Magnaporthe.*

Applicants respectfully assert that the rejection of Claims 8 and 13, as amended, as being anticipated by Bode et al. is incorrect, as Bode et al. fail to teach every element of Applicants' claimed invention. Bode et al. teach an assay for the identification of an inhibitor of a *Candida* 3-isopropylmalate dehydratase, but fail to teach identification of an inhibitor of a *Magnaporthe* 3-isopropylmalate dehydratase as taught by Applicants' claimed invention. The teachings of Bode et al. would not have implicitly or explicitly suggested to one of ordinary skill in the art, at the time the application was filed, that an inhibitor of a *Candida* 3-isopropylmalate dehydratase would also inhibit a *Magnaporthe* 3-isopropylmalate dehydratase, as Bode states that "[i]n yeasts and fungi, knowledge of the kinetic and regulatory properties of the enzyme is not extensive and includes only *Saccaromyces cerevisiae* and *Neurospora crassa.* From studies with these organisms it has been documented that there are similarities but also differences of the enzyme properties." (Bode et al., page 21, lines 15-19). Because of the uncertainty of the effect of a pathway disruption in a particular fungus, Bode et al. (examining *Candida)* cannot be applied to Applicants' finding (in *Magnaporthe*). Therefore, Applicants respectfully assert that it is not possible for Bode et al. to anticipate Applicants' claimed invention, as Bode et al. fail to teach every element of Applicants' claimed invention. Accordingly, withdrawal of the 35 U.S.C. § 102(b) rejection of Claims 8 and 13 is respectfully requested.

Claim 13 is also rejected under 35 USC § 102(b) as anticipated by Grandoni with evidence from IUBMB Enzyme Nomenclature Classification. Applicants respectfully assert that the rejection of Claim 13, as amended, as being anticipated by the Grandoni reference with evidence from IUBMB Enzyme Nomenclature Classification is incorrect, as the reference fails to teach every element of Applicants' claimed invention. The Grandoni reference teaches a method to identify an inhibitor of isopropylmalate isomerase from the bacterial strain *Mycobacterium*, and as discussed above for the Bode reference, it is not possible to predict the outcome of disruption of a particular pathway in a fungus based on the results of such a disruption in a second fungus, so it is certainly not reasonable to expect that the result of a disruption in a bacterial strain (the

Mycobacterium of Grandoni) would be the same as the result of a disruption in a fungal strain (the *Magnaporthe* of Applicants' claimed invention). Therefore, withdrawal of the 35 U.S.C. § 102(b) rejection of Claim 13 is respectfully requested.

Claim 13 is also rejected under 35 USC § 102(b) as anticipated by Hawkes et al. with evidence from IUBMB Enzyme Nomenclature Classification. Applicants respectfully assert that the rejection of Claim 13, as amended, as being anticipated by the Hawkes reference with evidence from IUBMB Enzyme Nomenclature Classification is incorrect, as the reference fails to teach every element of Applicants' claimed invention. As discussed *supra* for the Bode reference and the Grandoni reference, the Hawkes reference provides data from bakers yeast (enzyme assays) and carrot cells (growth inhibition tests), and it is not possible to predict the outcome of such data in a fungus not assayed (such as the *Magnaporthe* of Applicants' claimed invention). Hawkes notes that "[t]he observations in this paper indicate that **herbicidal** activity is also possible through inhibiting the biosynthesis of leucine alone, and more specifically, through inhibiting isopropylmalate isomerase" (Hawkes et al., page 367, column 2, lines 4-8, emphasis added). Even the title of the Hawkes paper, "A Herbicidal Inhibitor of Isopropylmalate Isomerase," indicates the herbicidal focus of the results reported by Hawkes et al. The Hawkes reference does not speak to inhibitors of a *Magnaporthe* 3-isopropylmalate dehydratase/isopropylmalate isomerase. Therefore, withdrawal of the 35 U.S.C. § 102(b) rejection of Claim 13 is respectfully requested.

III. Claim Rejections - 35 USC § 103(a)

Claims 8-9, 13-14, and 18-19 are rejected under 35 USC § 103(a) as obvious over Bode et al., Grandoni, and Hawkes et al. in view of Rubin et al. Claims 9, 14, and 18-19 are herein cancelled. Applicants respectfully request reconsideration of the rejection of Claims 8 and 13 in light of the amendment to the claims and the remarks that follow.

To establish a *prima facie* case of obviousness, the Patent Office must satisfy that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. In re Skinner, 2 USPQ2d 1788, 1790 (Bd. Pat. App. & Int. 1986). *Prima facie* obviousness cannot be

established by combining the teachings of the prior art to produce the claimed invention in the absence of such a teaching, suggestion, or incentive supporting the combination. In re Geiger, 2 USPQ2d 1276 (Fed. Cir. 1987). Moreover, the mere fact that references can be combined does not render the combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 16 USPQ2d 1430 (Fed. Cir. 1990, emphasis added); In re Fritch, 23 USPQ2d 1780 (Fed. Cir. 1992). In the case of Mills, the Court of Appeals for the Federal Circuit reversed the Patent Office finding of obviousness, holding that while the prior art invention was capable of being modified to achieve the claimed invention, there was no suggestion of the desirability of the modification within the prior art reference itself. Mills, 16 USPQ2d at 1432 (emphasis added).

Another requirement for a finding of obviousness is that the prior art reference or combination of references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (CCPA 1970) ("All words in a claim must be considered in fudging the patentability of that claim against the prior art."). A statement by the Patent Office that modifications of the prior art to meet the claimed invention would have been well within the ordinary skill of the art at the time the claimed invention was made, because the references teach that all aspects of the claimed invention were individually known in the art, is not sufficient to establish a *prima facie* case of obviousness, without some objective reason to combine the teachings of the references. Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Moreover, it is not relevant that any individual element of the claimed invention was known in the art. Jones v. Hardy, 220 USPQ 1021,1024 (Fed. Cir. 1984) ("[I]t is irrelevant in determining obviousness that all or other aspects of the claim may be well known in the art.").

In light of the foregoing, Applicants respectfully submit that amended Claims 8 and 13 are not obvious in view of the cited references. The combination of Bode et al., Grandoni, and Hawkes et al. in view of Rubin et al. is improper, as there is no suggestion of the desirability within the prior art references. Applicants' amended Claim 8 is directed to a method for identifying a test compound as a candidate for an antibiotic, wherein a 2-Isopropylmalate is contacted with a *Magnaporthe* 3-Isopropylmalate dehydratase, a 2-Isopropylmalate is contacted with a *Magnaporthe* 3-Isopropylmalate

dehydratase and a test compound, and a change in concentration is determined for at least one of the following: 2-Isopropylmalate, H_2O, and/or 3-Isopropylmalate, where a change in concentration for any of the above substances indicates the test compound is a candidate for an antibiotic. Applicants' amended Claim 13 is directed to a method for identifying a test compound as a candidate for an antibiotic, wherein a 3-Isopropylmalate is contacted with a *Magnaporthe* 3-Isopropylmalate dehydratase, a 3-Isopropylmalate is contacted with a *Magnaporthe* 3-Isopropylmalate dehydratase and a test compound, and a change in concentration is determined for at least one of the following: 2-Isopropylmalate, H_2O, and/or 3-Isopropylmalate, where a change in concentration for any of the above substances indicates the test compound is a candidate for an antibiotic.

The Examiner is relying on a combination of four references in support of the present obviousness rejection. Applicants assert that the present invention is non-obvious over Bode et al., Grandoni, and Hawkes et al. in view of Rubin et al., because even with knowledge of the present invention, the Examiner had to rely on a multiplicity of references and pick and choose among the features of those references, to come up with elements of the claimed invention, and even then could not provide each and every element of the present claimed invention. No one skilled in the art, so far as the references cited by the Examiner are concerned, thought of making this combination, as evidenced from the multiplicity of references that are necessary to make the rejection.

The Examiner cites that Bode et al., Grandoni, and Hawkes et al. teach identification of an inhibitor of 3-isopropylmalate dehydratase, but, as discussed *supra*, none of them address identification of inhibitors of a *Magnaporthe* 3-isopropylmalate dehydratase. None of the references mention *Magnaporthe* in any way, and when multiple organisms are discussed in a general way (Bode et al., page 21 lines 15-19) both similarities and differences among their leucine biosynthesis pathways are mentioned, indicating that assay results are not predictable and thus drawing into question a reasonable expectation of success without benefit of the knowledge provided by Applicants' claimed invention. The Rubin reference is no longer proper, as Claims 18-19 are herein canceled. Applicants assert that the Examiner has not provided evidence for a *prima facie* case of obviousness and therefore, withdrawal of the 35 U.S.C. § 103(a) rejection of Claims 8 and 13 is respectfully requested.

IV. Concluding Remarks

Applicants respectfully submit that Claims 8, 11, 13, and 16 as amended are in condition for allowance. Accordingly, reconsideration of the application and passage to allowance are respectfully solicited. Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned agent so that further examination of this application can be expedited.

Respectfully submitted,

Deborah H. Spencer

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Deborah H. Spencer
Registration No. 50,468
(phone) 919-425-3035
(fax) 919-485-0812

Paradigm Genetics, Inc.
108 Alexander Drive
RTP, NC 27709

Customer No. 022881